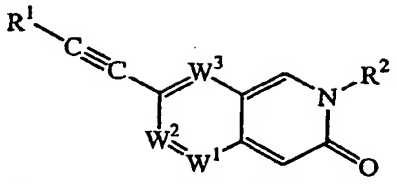
CLAIMS

What is claimed is:

1. A compound of Formula II



II

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is independently selected from:

C_5 or C_6 cycloalkyl-(C_1-C_8 alkylenyl);

Substituted C_5 or C_6 cycloalkyl-(C_1-C_8 alkylenyl);

C_8-C_{10} bicycloalkyl-(C_1-C_8 alkylenyl);

Substituted C_8-C_{10} bicycloalkyl-(C_1-C_8 alkylenyl);

5- or 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobicycloalkyl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobicycloalkyl-(C_1-C_8 alkylenyl);

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Naphthyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl); and

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5- or 6-membered heteroaryl;

Substituted 5- or 6-membered heteroaryl;

8- to 10-membered heterobiaryl;

Substituted 8- to 10-membered heterobiaryl;

R^2 is independently selected from:

H;

C_1-C_6 alkyl;

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Naphthyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl); and

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Phenyl-O-(C_1-C_8 alkylenyl);

Substituted phenyl-O-(C_1-C_8 alkylenyl);

Phenyl-S-(C_1-C_8 alkylenyl);

Substituted phenyl-S-(C_1-C_8 alkylenyl);

Phenyl-S(O)-(C_1-C_8 alkylenyl);

Substituted phenyl-S(O)-(C_1-C_8 alkylenyl);

Phenyl-$S(O)_2$-(C_1-C_8 alkylenyl);

Substituted phenyl-$S(O)_2$-(C_1-C_8 alkylenyl);

Each substituted R^1 and R^2 group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C_1-C_6 alkyl;

CN;

CF_3;

HO;

(C_1-C_6 alkyl)-O;

(C_1-C_6 alkyl)-$S(O)_2$;

H_2N;

(C_1-C_6 alkyl)-N(H);

(C_1-C_6 alkyl)$_2$-N;

(C_1-C_6 alkyl)-C(O)O-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)O-(1- to 8-membered heteroalkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)N(H)-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylenyl)$_m$;

$H_2NS(O)_2$-(C_1-C_8 alkylenyl);

(C_1-C_6 alkyl)-N(H)$S(O)_2$-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)$_2$-$NS(O)_2$-(C_1-C_8 alkylenyl)$_m$;

3- to 6-membered heterocycloalkyl-(G)$_m$;

Substituted 3- to 6-membered heterocycloalkyl-(G)$_m$;

5- or 6-membered heteroaryl-(G)$_m$; and

Substituted 5- or 6-membered heteroaryl-(G)$_m$;

(C_1-C_6 alkyl)-$S(O)_2$-N(H)-C(O)-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)-N(H)-$S(O)_2$-(C_1-C_8 alkylenyl)$_m$;

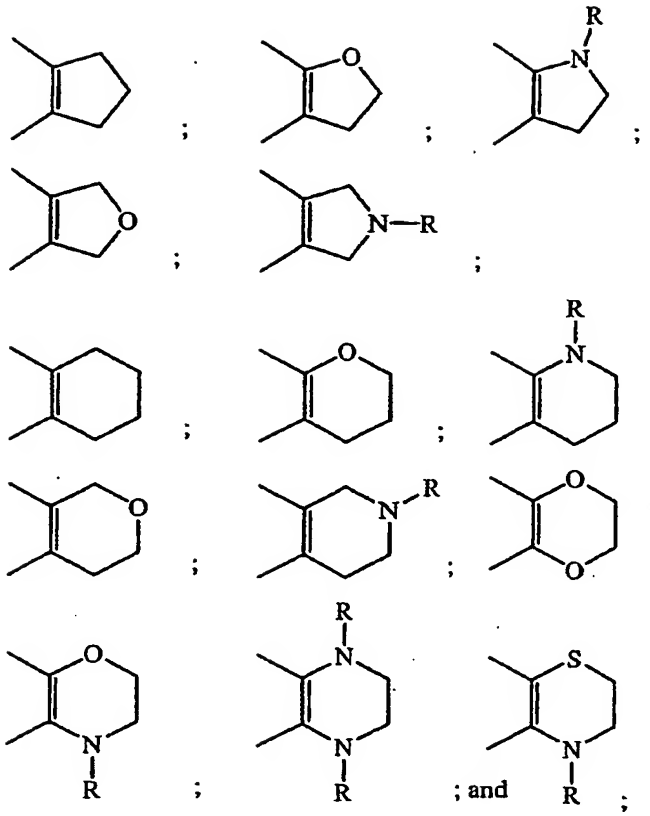
wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

HO_2C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



R is H or C_1-C_6 alkyl;

G is CH_2; O, S, S(O); or $S(O)_2$;

Each m is an integer of 0 or 1;

Each W^1, W^2, and W^3 is independently N or C-R^4;

R^4 is H, C_1-C_6 alkyl, H_2N, HO, or halo;

wherein each C_8-C_{10} bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic

rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 $N(C_1$-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 $N(C_1$-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 $N(C_1$-C_6 alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and $N(C_1$-C_6 alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 $N(C_1$-C_6 alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any $(C_1\text{-}C_6 \text{ alkyl})_2\text{-}N$ group, the $C_1\text{-}C_6$ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, selected from:

4-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid tert-butyl ester;

4-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid;

2-(3,5-Difluoro-4-hydroxybenzyl)-7-[3-(4H-[1,2,3]triazol-4-yl)prop-1-ynyl]-2H-isoquinolin-3-one;

7-(3-Phenyl-prop-1-ynyl)-2-(4-trifluoromethylbenzyl)-2H-isoquinolin-3-one;

2-(3-Fluorobenzyl)-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-3-one;

4-[7-(3-Imidazol-1-ylprop-1-ynyl)-3-oxo-2H-isoquinolin-2-ylmethyl]benzoic acid tert-butyl ester;

4-[7-(3-Imidazol-1-ylprop-1-ynyl)-3-oxo-2H-isoquinolin-2-ylmethyl]benzoic acid;

3-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzonitrile;

4-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzenesulfonamide;

4-[3-Oxo-7-(3-[1,2,3]triazol-1-ylprop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid tert-butyl ester;

4-[3-Oxo-7-(3-[1,2,3]triazol-1-ylprop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid;

4-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid methyl ester;

3-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid methyl ester;

2-(4-Fluorobenzyl)-7-3-phenylprop-1-ynyl-2H-isoquinolin-3-one;

7-(3-Phenylprop-1-ynyl)-2-(3-trifluoromethylbenzyl)-2H-isoquinolin-3-one;

2-(3-Chlorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one;

2-(3,4-Difluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one; and

4-[1-Oxo-7-(3-[1,2,4]triazol-1-ylprop-1-ynyl)-2H-isoquinolin-3-ylmethyl]benzoic acid tert-butyl ester; or

a pharmaceutically acceptable salt thereof.

3. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

4. A method for treating osteoarthritis, comprising administering to a patient suffering from osteoarthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

5. A method for treating rheumatoid arthritis, comprising administering to a patient suffering from rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.